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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/814,293
Filing Date: April 01, 2004
Appellant(s): STARK ET AL.

Sarah Klosek
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 27 July 2009 appealing from the Office action mailed 26 November 2008.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is incorrect. A correct statement of the status of the claims is as follows:

The Appeal Brief filed 27 July 2009, states that claims 1-32 are pending. The brief later requests that the claims as amended after final rejection, also filed 27 July 2009, be entered on the record. Appellants' amendment has been entered via Supplemental Advisory Action on 25 February 2010. Per the amendment, claims 10-14 have been canceled. This appeal now involves claims 1-9 and 15-32.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is incorrect.

The amendment after final rejection filed on 27 July 2009 has been entered via Supplemental Advisory Action on 25 February 2010.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. The changes are as follows: It should be noted and clarified that two separate rejections under the second paragraph of 35 USC 112, were actually set forth in the Final Rejection. The first of these two is addressed below.

WITHDRAWN REJECTIONS

The following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner.

The first of the two aforementioned rejections is directed specifically to claim 1 where it is argued that "claim 1 recites the broad recitation "Eudragit poly acrylic acid", and the claim also recites "Eudragit S and Eudragit L" which are narrower statements of the range/limitation."

The Examiner withdraws this rejection.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

5,137,733	Noda et al.	8-1992
5,580,578	Oshlack et al.	12-1996

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

CLAIM REJECTIONS - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Noda et al. (U.S. Patent 5,137,733) in view of Oshlack et al. (U.S. Patent 5,580,578).

The instant claims 1, 2, 26, 27 and 30 are drawn to a multiparticulate bisoprolol formulation wherein each particle comprises a core of bisoprolol or a pharmaceutically acceptable bisoprolol salt surrounded by a release-controlling, polymeric coating. Claims 3 and 28 further limit the drug to a pharmaceutically acceptable salt of bisoprolol (e.g. bisoprolol fumarate or hemifumarate). Dependent claims 4 and 29 further limit the bisoprolol salt of claim 3 to bisoprolol hemifumarate. Claims 5 and 6 recite *in vitro* release profile limitations to the formulation. Claims 7 and 8 further limit the composition of claim 1 such that a sealant is applied to the medicated core prior to application of the polymeric coating. Claim 9 further limits the formulation such that the bisoprolol active ingredient is applied to a core particle (e.g. non-pareil seed) having an average diameter between 400 and 1100 microns. Claims 10 and 11 further limit the polymeric coating of claim 1 wherein the polymer of claim 10 is a major proportion of the coating with low permeability and claim 11 is a minor proportion of the coating with high permeability. Claim 12 further limits the coating of claim 10 such the at least one of polymers is a methacrylic acid copolymer. Claim 13 further limits the coating of claim 10 such the at least one of polymers is a ammonio methacrylate copolymer. Claim 14 further limits the polymer coating of claim 12 such that a mixture of polymers is used. Dependent claim 15 further limits the polymer coating by including one or more soluble excipients. The soluble excipients are further limited by category in (e.g. soluble polymer, surfactant, etc.) in claim 16 and by compound (e.g. PVP, PEG, and mannitol) in claim 17. Claim 18 further limits the soluble excipient of claim 15 such that the excipient is present between 1-10% by weight based on the total dry weight of the polymer. Claim 19 recites the addition of one or more auxiliary agents to the polymer coating. Claims 20 and 21 further limit the formulation of claim 1, such

that the polymer coating contributes to the overall formulation, a given weight percentage of the core. Claim 20 recites a 10-100% weight gain on the core whereas claim 21 recites a 25-70% contribution. Claim 22 further limits the formulation of claim 1 (see Claim Objections above), such that a sealant is applied to the polymeric coating. Claim 23 recites useable examples for said sealant. Claim 24 recites different oral dosage forms that may encompass the bisoprolol formulation. Claim 25 further limits the type of tablet form of the formulation (e.g. disintegrating, effervescent, etc.). Claims 31 and 32 further limit the composition of claim 26 to particular amounts of bisoprolol.

Noda teaches a controlled release pharmaceutical preparation comprising a core containing a medicinal compound and a coating layer containing a water-repellant salt and a water-insoluble and slightly water-permeable acrylic polymer having a methacrylic copolymer group (claim 1). Example 12 teaches the medicinal agent to be bisoprolol fumarate. Noda also teaches that the system is designed to have an initial lag period before the medicinal agent is released or dissolved and that this initial period can be varied depending upon the number of coating layers applied to the cores (col. 5, lines 19-56). Further, the preparation can retain an effective blood concentration for many hours and can again differ with the amount of layers applied to the cores (col. 5, lines 19-56). The preparation is suitable for a once-a-day administration (col. 6, lines 1-2). The website: http://pharmacycode.com teaches that the hemifumarate salt and fumarate salt have the same formula and structures. Non-pareil seeds (e.g. spherical particles) are taught to have a mean diameter between 500 and 1000 microns (col. 3, lines 16-18). Fillers, as defined by Appellant (pg. 14, lines 13-14), include magnesium stearate and calcium stearate, both of which Noda teaches in claim 1 as being part of the coating.

An additional coating layer is added to the cores after the acrylic polymer layer (col. 2, lines 32-39). The acrylic polymers are taught at col. 2, lines 40-59 and include Eudragit RS as well as a combination of Eudragit RS and RL. Example 6 teaches a coating layer with the Eudragit RS/RL combination. The additional coating layer is chosen from compounds such as hydroxypropyl cellulose (col. 2, lines 60-66). The amount of coating layer is about 5% to about 80% based on the weight of the core (col. 3, lines 11-21). Various excipients such as polyvinylpyrrolidone and mannitol are present in the core (col. 3, lines 37-57). The acrylic coating layer is further taught to comprise plasticizers (col. 4, lines 43-55). Still further, Noda teaches formulations with differing number of coating layers wherein the lag time and complete dissolution are different. Preparation (b) of Figure 1, prepared as polymer coated granular tablets in Test Example 1, exemplifies the dissolution profile of the instant claims.

While Noda teaches many of the limitations of the instant claims, the exact composition of the instant claims is not exemplified in the reference. That which is not expressly taught by Noda includes: application of the sealant is to the core prior to the application of the polymeric coating, the percent soluble excipient used (e.g. 1-10%), the percent weight contributions to the overall composition by the polymeric coating, and the amount of bisoprolol added to the composition.

Oshlack et al. teaches a controlled release formulation wherein a barrier layer is incorporated between the medicinal core and the acrylic coating layer (col. 13, line 62 to col. 14, line 2). The barrier layer can be hydroxypropyl methylcellulose or any film-forming agent known in the art (col. 13, line 62 to col. 14, line 2). Eudragit RS/RL dispersions mixed together in the desired ratios are taught as the polymer coatings (col. 9, lines 47-54).

In view of the combined teachings of the prior art, one of ordinary skill in the art would have been motivated to prepare a controlled release system comprising bisoprolol fumarate in a core coated first, by a barrier layer and second by an acrylic polymer with a reasonable expectation of successfully obtaining the desired dissolution pattern of the drug from the dosage. Oshlack et al. teach that it may be desirable to obtain the desired efficacy by utilizing different coating components to effect an overall release of the active agent within the desired levels over a longer period of time (col. 18, lines 3-11). Therefore, modification of the instant dosage formulation to apply the barrier layer (e.g. hydroxypropyl methylcellulose) prior to applying the polymeric coating, as earlier defined, is well within the purview of the skilled artisan.

Furthermore, it is *prima facie* obvious to switch the order of addition of said barrier and polymeric layer(s) to the formulation with the result being that of the controlled release composition of Appellants' instant claims 1-32. The basis for this *prima facie* obviousness rejection can be found in the following case law: *In re Burhans*, 154 F.2d 690, 69 USPQ 330 (CCPA 1946), wherein selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results; and *In re Gibson*, 39 F.2d 975, 5 USPQ 230 (CCPA 1930), wherein selection of any order of mixing ingredients is *prima facie* obvious.

Neither reference teaches the percentage of soluble excipient included in the polymeric coating (e.g. 1-10%), the percent weight gain of the formulation contributed by the polymeric coating (e.g. 10-100% and 25-70%) or the amount of bisoprolol added to the formulation (claims 31 and 32) as claimed by the Appellants. Since the value of each parameter with respect to the claimed dosage form is adjustable, it follows that each is a result-effective parameter that a person having ordinary skill in the art would routinely optimize. Optimization of parameters is a

routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of bisoprolol to add to the dosage formulation as well as the optimal percentages of coating and excipient to include in order to best achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, optimization of any of these ingredient amounts would have been obvious at the time of Appellants' invention.

CLAIM REJECTIONS - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Appellants regard as the invention.

Claim 1 contains the trademark/trade name "Eudragit®". Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe: poly

acrylic acid, L-, and S-type polyacrylic compounds and, accordingly, the identification/description is indefinite.

(10) Response to Argument

Rejection under 35 USC 103(a)

Appellants argue that "Noda et al. does not disclose or suggest a bisoprolol formulation that includes at least one enteric polymer coating material selected from the group recited in claim 1." Appellants further point out that Noda et al. is expressly directed to the use of pH-independent acrylic polymers which include trimethylammoniumethyl groups or the "RS" and/or "RL" blends of the trademarked product Eudragit® [emphasis added]. Appellants argue that the instant invention is distinct from the Noda reference because Noda exclusively employs pH-dependent rather than pH-independent polymers [emphases added]. Concerning the subsequent combination of the Oshlack reference with Noda et al., Appellants argue that despite Oshlack disclosing the incorporation of the instantly claimed barrier layer between the medicinal core and the acrylic coating layer, such a teaching "does not guide one of skill in the art to a pH-dependent polymer system as presently claimed."

The Examiner respectfully disagrees. The claim recites that particles of the active ingredient bisoprolol or one of its pharmaceutically acceptable salts, be surrounded by a polymeric coating. The limitations for the coating as recited by Appellants is that it comprise at least one enteric polymer coating material which is selected from the Markush group recited by claim 1. Said group recites the generic compound Eudragit poly acrylic acid, in addition to Eudragit S and Eudragit L. The term "enteric" as it relates to a polymer coating, is broadly and

reasonably interpreted by the Examiner from Appellants' instant disclosure as a recitation of a polymer coating which when applied results in a "delayed" release of the active ingredient it covers. The term is not interpreted by the Examiner as distinguishing between "pH-dependent" and "pH-independent". It thus stands to reason that Appellants' recitation of the genus "Eudragit poly acrylic acid" as a limitation of an "enteric polymer coating" material similarly does not distinguish between "pH-dependent" and "pH-independent".

Noda et al. teaches in Example 10 that fine powder particles of nicotinamide were coated using Eudragit RS. This teaching is relevant to Example 12 since the same procedure is performed with the exception that bisoprolol fumarate is substituted for nicotinamide as the active ingredient. Thus, Noda et al. expressly teach the preparation of bisoprolol particles coated with Eudragit RS. Eudragit "RS" and "RL", per Appellants' instant disclosure are empirically and alternatively defined as "ammonio methacrylate copolymers" and thus fall within the genus of Eudragit polyacrylic acids (see pg. 10, lines 7-9). As such, the Examiner respectfully points out that the limitations set forth in the instant claim, broadly and reasonably interpreted, do not preclude the use of a pH-independent polymer such as Eudragit RS or RL for use as the enteric coating material.

The Examiner also respectfully disagrees with Appellants' arguments directed towards Oshlack. The Oshlack reference is directed to the same technology, namely a stable solid controlled release formulation having a coating derived from an acrylic polymer. Preferred teachings of the polymer coating include blends of the aforementioned Eudragit "RS" and "RL" (col. 9, lines 47-54). It is further taught by the reference that other embodiments of the invention will use hydrophobic acrylic polymers as the polymer coating such as Eudragit "L" or "S" (col.

10, lines 6-26). Oshlack further discloses that the motivation to modify the acrylic polymer coating lay in selecting the desired permeability properties (and thus the dissolution profile) of the final formulation (col. 10, lines 27-34).

Thus, the teachings of Noda et al., either alone or in combination with Oshlack et al. would have motivated a person of ordinary skill in the art, to not only have prepared the multiparticulate bisoprolol composition as claimed, but to have further modified said coating in order to achieve a more specific formulation, namely a multiparticulate bisoprolol formulation having an enteric, pH-dependent polymeric coat.

Rejection under 35 USC 112, ¶2

Appellants argue in accordance with MPEP §2173.05(u) that the use or presence of a trademark or tradename in a claim is not, *per se*, improper under 35 USC 112, but the claim should be carefully analyzed to determine how the mark or name is used in the claim. Appellants further argue that the terms "Eudragit polyacrylic acid", "Eudragit S" and "Eudragit L" are used in claim 1 to identify a specific manufacturer of the enteric polymer coating material and enteric polyacrylic acid, whose polymers are given fixed and definite meanings by the manufacturer.

The Examiner respectfully disagrees with Appellants argument that the use of the tradename or mark provides a fixed and definite meaning to the enteric polymer coating material, particularly where it pertains to the polyacrylic acid. The second paragraph of MPEP §2173.05(u) further adds the following:

> **If the trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with**

> **the requirements of the 35 USC 112, second paragraph.** *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. In fact, the value of a trademark would be lost to the extent that it became descriptive of a product, rather than used as an identification of a source or origin of a product. Thus, the use of a trademark or trade name in a claim to identify or describe a material or product would not only render a claim indefinite, but would also constitute an improper use of the trademark or trade name.

It appears to the Examiner that Appellants are attempting to further limit the enteric polymer coating of the particle composition in terms of a particular material, namely as a Eudragit polymer. Thus, despite having fully considered the presence and use of the mark, as it pertains to the "polyacrylic acid", "S" and "L" formulations of Eudragit®, the scope of the claim remains unclear.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Jeffrey T. Palenik/

Examiner, Art Unit 1615

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/Ardin Marschel/

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